GP255
#15

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS



In re Application of:
Shepherd, et al.

Filed: February 23, 1989

Serial No. 07/313,911

For: METHOD AND APPARATUS FOR DIRECT MEASUREMENT OF HEMOGLOBIN SPECIES IN WHOLE BLOOD

Examiner: R. Rosenberger

Group Art Unit: 255

Atty. Dkt.: UTSK:097/BAH

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on July 26, 1991
(Date of Deposit)
Kevin L. Daffer
Name of applicant, assignee or Registered Representative
Signature
July 26, 1991
Date of Signature

92-0991

**APPEAL BRIEF**

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

Further to the Notice of Appeal filed February 27, 1991, Appellants present this Appeal Brief. The period for filing this Appeal Brief having expired April 27, 1991, filed herewith is a Petition for Extension of Time, with the appropriate fee, extending the time period for filing this Appeal Brief for three months to and including July 27, 1991. The only issue presented in this appeal is the non-obviousness of the appealed claims over the art of record under 35 U.S.C. § 103.

ok refund 365.00
ok refund 120.00 jlc

DS20044 08/05/91 07313911 01-2508 020 217 365.00CH
DS20045 08/05/91 07313911 01-2508 020 220 120.00CH

P 30131 08/07/91 07313911 01-2508 030 217 365.00CR
P 30132 08/07/91 07313911 01-2508 030 220 120.00CR

## TABLE OF CONTENTS OF APPELLANTS' BRIEF

## 1. STATUS OF CLAIMS

Claims 1-14 were originally filed in this case, and claim 15 was later added. Claims 13, 14 and 15 have been canceled leaving only claims 1-12 in this application. Appellants appeal from the Final Rejection of claims 1-12. A copy of claims 1-12 on appeal is included in the Appendix hereto.

## 2. STATUS OF AMENDMENTS

The amendment filed July 3, 1990, adding claim 15 and amending claims 1, 11, 12, 13 and 14, has been entered.

The amendment after final rejection filed January 25, 1991, cancelling claims 13, 14 and 15, and further amending claim 1, has also been entered.

The Appendix hereto presents claims 1-12 after entry of these two amendments.

## 3. SUMMARY OF THE INVENTION

The invention, as disclosed in the subject application, relates to the measurement of three of more species of hemoglobin in whole, undiluted blood. By radiating a thin sample of whole, undiluted blood with selected wavelengths of radiation, optical densities can be measured which are linearly related to hemoglobin concentration (Fig. 5).

Of importance is the process by which radiation wavelengths are chosen. Wavelengths are selected 1) to maximize their absorbance through the whole blood sample, 2) to distinguish one hemoglobin species from another, and 3) to minimize the sensitivity of the molar extinction coefficients of the hemoglobin species due to small changes in radiation wavelength (claim 1; Figs. 4 and 5). Careful selection of radiation wavelengths, as well as efficient sizing of the test device, establishes a substantially linear relationship between the optical densities and hemoglobin concentrations for each hemoglobin species.

Test device sample size is typically in the range of 80 to 150 micrometers with an approximately 600 square millimeters detecting area placed within 2 to 10 millimeters from the sample (claims 2-4; specification: page 8, lines 21-24). By careful attention to test geometry, detecting can occur through approximately 70° radiation angle emanating from the sample (claim 5; specification: page 8, lines 24-27).

Carefully selected radiation wavelengths are generated using either interference filters (claim 6; specification: page 7, line 29), tunable lasers (claim 7; specification: page 8, line 1), light-emitting diodes (claim 8; specification: page 8, line 3), a controllable monochromator (claim 9; specification: page 7, lines 32-33), or a controllable diffraction grating (claim 10; specification: page 7, line 33). By impinging a plurality of carefully selected radiation frequencies (at least three frequencies) upon the sample containing whole undiluted blood,

concentrations of at least three constituent components can be calculated using the Beer-Lambert Law of absorption spectroscopy (claims 11-12; Fig. 4; specification: page 9, lines 18-29).

The present invention therefore minimizes deleterious scattering effects and discriminates between each species by selecting radiation frequencies and optical geometries which provide a linear relationship necessary for accurately measuring concentrations of three or more constituent components of whole, nonhemolyzed blood.

## 4. ISSUES

1. Whether the *Anderson et al.* reference in combination with the *Brown et al.* reference render claims 1, 2 and 6-12 obvious under 35 U.S.C. § 103

2. Whether the *Anderson et al.* and *Brown et al.* references in combination with the *Shibata et al.* reference render claims 3-5 obvious under 35 U.S.C. § 103

## 5. GROUPING OF CLAIMS

Claims 1 and 8-12 are separately patentable. Claims 2-7 stand or fall with claim 1. Appellants present reasons why claims 1 and 8-12 are separately patentable and do not stand or fall together under the appropriate parts of the following argument.

## 6. ARGUMENT

### A. SUMMARY OF APPELLANTS' ARGUMENT

The Appellants' invention exemplifies a non-obvious method of determining concentrations of at least three constituent components of a whole, undiluted blood sample (claim 1). By irradiating a whole blood sample, the present invention can measure the concentrations of at least three constituent components. According to the present invention, it is important that radiation frequencies be selected which minimize scattering effects which normally occur when light strikes red blood cells. By selecting input frequencies that are absorbed rather than scattered, a linear relationship exists between the measured optical density and the concentration of constituent component being measured. A large detecting area approximately 600 square millimeters (claim 3) is placed within 2 to 10 millimeters from the sample (claim 4) to capture any scattering which might occur.

According to the present invention, radiation frequencies are chosen not only to minimize deleterious scattering effects, but also to distinguish each constituent species from one another (claim 1). In this way, when the operator chooses a specific radiation frequency, he or she knows that the resultant optical density reading is directed to a particular constituent component or species.

The Examiner cited and applied three references: *Anderson et al.*, *Brown et al.*, and *Shibata et al.* The Examiner asserts that the combination of *Anderson* and *Brown* renders claim 1 obvious. The Examiner further asserts that it would be obvious to use the data of *Anderson* to calculate concentrations of at least three components of blood as shown by *Brown*. In response thereto, Appellants assert that even if the hypothetical combination could be made, neither *Anderson* nor *Brown* teach the art of selecting frequencies to minimize deleterious scattering effects and to distinguish one constituent species from another as required by claim 1. While *Anderson* teaches that scattering predominates at wavelengths or frequencies with low extinction coefficients (*Anderson* - Fig. 2 and page 177), *Anderson* does not suggest that scattering effects are a function of only the frequency selected or that certain frequencies produce better results when targeted to a certain constituent component. Furthermore, *Brown* makes no mention whatsoever to indicate that the data taken in *Anderson* can be used to calculate the concentrations of at least three species.

Thus, not only does the hypothetical combination fail to meet the limitations of claim 1, but there is no suggestion in either *Anderson* or *Brown* for making the hypothetical combination. Further, since *Anderson* deals specifically with whole, undiluted blood and *Brown* deals specifically with diluted, hemolyzed blood, each of their intended functions would be destroyed if the hypothetical combination were made. Appellants assert there would be

a disincentive for making the combination, since one reference (*Anderson*) clearly teaches away from the other reference (*Brown*), and vice versa.

The Examiner further asserts that detector size and location disclosed in *Shibata et al.* would have been obvious for use with *Anderson* and *Brown* for solving the problems of light scatter using selected test geometries as recited in claims 3-5 in the subject application. In response thereto, Applicants first assert that *Shibata* deals with non-analogous art, separate and distinct from blood analyzer art. Secondly, *Shibata* does not cure the inherent incompatibility of *Anderson* and *Brown* described in the previous paragraph. Thirdly, the hypothetical combination of *Shibata, Anderson* and *Brown* proposed by the Examiner does not meet the limitations of present claim 1 combined with claims 3-5.

The Appellants' creative approach of selecting a specific radiation frequency to measure a specific species or constituent component concentration is neither taught nor suggested in the hypothetical *Anderson*, *Brown* or *Shibata* combination. Furthermore, Applicants' approach of selecting radiation frequencies which do not scatter as they traverse the sample is also not disclosed in the hypothetical combination. Thus, proper application of Beer's law to predict each constituent component of three or more components or species using the present invention is not disclosed nor suggested in *Anderson*, *Brown* or *Shibata*.

Furthermore, Appellants assert that not only can the present invention accurately predict concentrations from Beer's law, but it can do so in a quick and efficient manner. The operator need not "prepare" the sample prior to study. Thus, the subject invention does not require dilution or hemolysis of the sample prior to study as in *Brown*. Furthermore, by targeting specific frequencies for specific constituent components, wherein the selected frequencies absorb rather than scatter, the present invention overcomes the disadvantages of *Anderson*. *Anderson* certainly does not make mention of frequencies chosen to minimize scattering. Instead, *Anderson* specifically teaches frequencies chosen which have high extinction coefficients as being those wavelengths which minimize scattering. Appellants assert that there are several wavelengths with low extinction coefficients which also may minimize scattering.

For the reasons stated above and for reasons further brought forth below, Appellants assert that claims 1-12 are possessed of individual and cumulative unique characteristics which impart patentability to the present invention. Therefore, each claim is in itself patentable apart from any of Appellants' other claims. In particular, the method of determining concentrations of at least three constituent components of whole blood of claim 1 is patentable as well as the optical configuration of claims 2-12 which are dependent thereon. Appellants urge the Examiner's rejection of these claims be reversed and the subject claims be allowed to issue.

## B. TABLE OF AUTHORITIES



## C. ARGUMENTS PRESENTED

Appellants' claim 1 specifies a method of determining concentrations of constituent components of whole, undiluted blood. Claim 1 is the only independent claim on appeal, and specifically refers to radiation frequencies which are selected to distinguish one constituent component from another and to minimize the effect of radiation scattering. Claims 2-12 are claims dependent from claim 1 and are directed toward the optical configuration and various methods used to generate radiation frequencies. Appellants assert that measurements of at least three consistent components of whole, undiluted blood using an

optical arrangement which minimize scattering is non-obviousness over the art cited by the Examiner for reasons cited below.

## I. Appellants' Claims 1, 2 and 6-12 Are Not Rendered Obvious Under 35 U.S.C. § 103 Over the Examiner's Cited References

### a. The Examiner's Rejections Under 35 U.S.C. § 103

In rejecting claims 1, 2 and 6-15 in the final Office Action, the Examiner specifically stated:

> Claims 1, 2 and 6-15 are rejected under 35 U.S.C. § 103 as being unpatentable over Anderson et al. taken with Brown et al. . . . It would have been obvious to use measurements from an instrument [Anderson] to calculate blood constituents because such use of optical absorbance for such calculations is known and such a use is at least suggested by the Anderson reference in its mention of the use of the data in and oxygen saturation measurement. . . . The use of data obtained from the device of Anderson et al. to calculate the concentrations of at least three constituents of blood would have been obvious because it is known, as shown by Brown et al. to use such data for such purposes.

### b. Appellants' Arguments/Response to First Issue

*Anderson et al.* reference (which teaches radiating whole, nonhemolyzed blood at high-extinction-coefficient frequencies to obtain two hemoglobin species) in combination with *Brown et al.* reference (which teaches radiating diluted hemolyzed blood at selected frequencies to obtain hemoglobin species) does not render claims 1, 2 and 6-12 "obvious" under 35 U.S.C. § 103.

Of course, the proper context for considering obviousness rejections is enunciated in Graham v. John Deere, 140 U.S.P.Q. 459 (1966). A proper Graham analysis includes:

1) a determination of the scope of the content of the prior art;

2) an analysis of the differences between the prior art and the claims at issue; and

3) a determination of the level of ordinary skill in the relevant art.

See, M.P.E.P. § 706.

**1) Determination of the Scope and Content of the Prior Art**

A determination of the scope and content of *Anderson* begins with the fact *Anderson* can only measure oxygenated and total hemoglobin content in whole blood and measurement appears limited to only those two blood constituents. Furthermore, *Anderson* uses the integrating sphere configuration to minimize scattering inherent when waves traverse whole blood. Still further, and of central importance to *Anderson*, is *Anderson's* observation that wavelengths with high extinction coefficients can achieve a dominant absorption pattern (page 177; Fig. 2). Thus, it is important in *Anderson* that wavelengths be chosen having high extinction coefficients in order to obtain a linear relationship between hemoglobin concentration and optical density (Fig. 2). Specifically, optical densities were studied in *Anderson* using

four different wavelengths, 505, 520, 530 and 560 nm. Fig. 6 of Anderson illustrates non-linearity obtained when 505 nm wavelength was used; Figs. 2 and 5 of Anderson illustrate the non-linearity obtained when 560 nm and 530 nm wavelengths, respectively, were used.

The scope of content of *Brown et al.* illustrates a device and method which can measure several constituent components (more than two but less than five). Although the ability to measure more than two components of blood represents a significant improvement over *Anderson*, *Brown* relies upon a complex device which must prepare the sample prior to radiation. In particular, *Brown* requires the sample to be both diluted and hemolyzed. Diluent from bottle 56 acts to dilute the blood before it is admitted to cuvette 34 (col. 13, line 39-col. 14, line 20). In addition, a mechanical hemolyzer 28 is connected to ensure the blood sample is hemolyzed as well as diluted (col. 6, lines 37-46). Thus, in order for *Brown* to achieve measurements of more than two constituent components, it must prepare the sample prior to measurement. *Brown* certainly does not suggest using whole, undiluted blood, nor does *Anderson* suggest using diluted, hemolyzed blood. In fact, the purpose of *Brown* is to prepare the sample in order to read more than three components. Appellants thereby assert the two references are mutually exclusive in their device and method of operation.

## 2) Analysis of the Differences Between the Prior Art and the Claims at Issue

In response to the reasoning behind the Examiner's rejections of claims 1, 2 and 6-15, as cited above, Appellant assert that (i) if the hypothetical combination of *Anderson* and *Brown* were capable of being made, this hypothetical combination, nevertheless cannot meet the limitation of the rejected claims, and in particular, claim 1; (ii) there is no suggestion in either *Anderson* or *Brown* for the hypothetical combination; and (iii) the Examiner's assertion that it would have been obvious to use the data of *Anderson* to calculate the concentrations of at least three components of blood as shown by *Brown*, is without support.

Assuming arguendo, that *Anderson* and *Brown* references can be combined as proposed in the Final Rejection, the limitations of claim 1 are nevertheless not met. Assuming the proposed combination describes a method of measuring at least three component constituents of whole blood, it does not allow the determination of constituent component concentrations at wavelengths chosen to minimize radiation scattering (claim 1). Furthermore, this combination does not suggest a method of generating radiation frequencies which distinguish one constituent component from another constituent component (claim 1). Constituents components are distinguished from each other in accordance with the present invention by using unique wavelengths which minimize the sensitivity of the molar extinction coefficients to small variations in the radiation wavelength. Neither

*Anderson* nor *Brown* or the combination of both *Anderson* and *Brown*, provide a method for minimizing scattering and for discriminating between each constituent component through the selection of radiation frequencies. Of importance in the claimed invention is the fact that it uses specific frequencies which demonstrate minimal amounts of scattering as they traverse the sample, and that the specific frequencies are chosen to measure corresponding specific constituent components.

The Examiner points to several wavelengths, 505, 520, 530 and 560, used by *Anderson* (*Anderson* - page 179) as being virtually identical with the range disclosed in the present application (page 7). In response thereto, Appellants assert that while these four wavelengths were studied in *Anderson*, not all of said four wavelengths demonstrate high extinction coefficients corresponding to minimal scattering. In particular, *Anderson* illustrates in Fig. 6 that results obtained using 505 nm wavelength are highly non-linear. Furthermore, results with a wavelength of 560 nm are also non-linear as shown in Fig. 2. It appears *Anderson* makes no assertion that wavelength 520 is linear or non-linear. Thus, while the present invention specifies certain wavelengths, including 506, 520 and 560 nm which substantially correspond to three wavelengths chosen in the *Anderson* study, these wavelengths would not produce satisfactory results in *Anderson* but would prove satisfactory in the present invention. In particular, *Anderson* shows at least two of these three wavelengths as having a significant scattering effect which

causes their non-linearity. Conversely, these three wavelengths are chosen in the present invention as having minimal scattering effects. Thus, the present invention renders a substantially linear relationship in three of the four wavelengths studied in Anderson, and which are generally shown in Anderson as being substantially non-linear. Further, Applicants strongly assert that while *Anderson* prefers wavelengths with high extinction coefficients to minimize scattering, there may be, in fact, certain wavelengths which have low extinction coefficients which also minimize scattering. As evidenced by the preferred wavelengths shown in Appellants' specification, certain wavelengths are chosen on page 7 (i.e., 506, 520 and 560 nm) which will minimize scattering in the present invention, but which do not minimize scattering in *Anderson*. Furthermore, and more importantly, *Anderson* makes no mention or even suggests that the wavelengths be chosen to distinguish constituent components as in the present claim 1.

In addition to *Anderson* not providing the essential method step of generating radiation frequencies which minimize radiation scattering and which distinguish constituent components, *Brown* does not even suggest any form of wavelength selection process whatsoever other than four wavelengths may be used, i.e., 535, 585.2, 594.5 and 526.6 nm (*Brown* - col. 3, lines 29-36). *Anderson* merely suggests minimizing scattering at wavelengths with high extinction coefficients -- a result dissimilar from the subject application wavelength selection process described above.

Thus, even if the hypothetical combination of *Anderson* and *Brown* were made, this combination could not provide the essential "generating" step of method claim 1. Unless there is some showing in either *Anderson* or *Brown* which indicates frequencies selected to minimize scattering and that these frequencies can be chosen to allow an operator to discriminate measurements obtained from one component from those measurements of another component, Applicants cannot see the Examiner's reasoning as to why the hypothetical combination of *Anderson* and *Brown* can meet the limitations of claim 1.

In the alternative, even if one can assume that the data obtained from *Anderson* can predict radiation frequencies which minimize scattering and which distinguish each constituent component as in claim 1, Applicants assert there is no suggestion made in either *Anderson* or *Brown* for the hypothetical combination proposed by the Examiner. There is no incentive for a skilled artisan to modify *Anderson* apparatus to that of *Brown* to achieve Appellants' claimed method.

The device and method of *Anderson* are used for estimating hemoglobin and oxygen concentrations in whole blood. *Anderson* uses an integrating sphere as its optical design of choice, preferably to minimize scattering inherent when waves impinge upon red blood cells found in whole blood. Conversely, *Brown* is directed to a complex device which prepares the sample by diluting and hemolyzing the blood to minimize the inherent effects of scattering in order to achieve readings on more than

two constituent components. Throughout the *Anderson* reference, mention is only made of total hemoglobin and oxygenated hemoglobin and measurement is limited to only those two blood constituents. Conversely, *Brown* mentions using only diluted and hemolyzed blood. In short, Appellants assert that there is no technological motivation for changing the whole blood apparatus of *Anderson* with the diluted, hemolyzed blood apparatus of *Brown*. In fact, Applicants assert that there would be a disincentive for making this modification since *Brown* clearly teaches that dilution and hemolysis is required for measuring more than two components. See In re Gordon, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984).

Even further, Applicants assert that even if there is some form of incentive for making this hypothetical combination established by the Examiner, "the references must expressly or impliedly suggest the claim combination or the Examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." Ex parte Clapp, 227 U.S.P.Q. 972, 973 (PTO Bd. App. 1985). In this regard, the Final Rejection has not made a *prima facie* case of obviousness as to why the proposed combination meets the limitations of claim 1, or that there is any suggestion for arriving at such a proposed combination. A *prima facie* case of obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion or

incentive supporting the combination." ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984). *Anderson* certainly does not suggest diluting its blood sample in order to achieve measurements of more than two constituent components. Conversely, *Brown* certainly does not suggest using whole, undiluted blood to achieve its readings. In fact, both references specifically require their blood conditions in order to achieve their stated purpose. Thus, Applicants must assert that the hypothetical *Anderson/Brown* combination cannot be made as proposed by the Examiner, and even if the proposed combination were made, said combination does not produce the claimed invention.

Finally, the Examiner's suggestion in the Final Rejection that it would have been obvious to use the data of *Anderson* to calculate the three components of blood as shown in *Brown*, is simply not supported by the record. *Anderson* certainly does not make any such suggestion, and to the contrary, *Brown* specifically avoids selecting wavelengths according to *Anderson* data. Certainly, *Brown* does not teach or suggest that the wavelengths used in its device be chosen having high extinction coefficients as proposed by *Anderson*. Still further, even if the data in *Anderson* could somehow be used by *Brown* to obtain at least three components of blood, the resulting combination of *Brown* and *Anderson* would not present radiation frequencies selected where absorbance is maximized and scattering is minimized in accordance with the claimed invention. The combination would merely present

high extinction coefficients and selected frequencies having said coefficients. Thus, Applicants must assert that there is no support for the Examiner's position that it would be obvious to use the *Anderson* data to calculate three components of blood as cited by *Brown*. *Brown* only shows what other researchers in hemoglobinometry have concluded that the way to produce the necessary linear relationship needed to analyze three or more components is to dilute and hemolyze the sample. For example, in addition to the *Brown et al.* patent, the *Raffaele* patent (U.S. Patent No. 4,013,417, filed July 31, 1975), requires hemolysis and dilution; the *Siggaard-Anderson* patent (U.S. Patent No. 4,308,029, filed May 5, 1980), requires chemical deoxygenation followed by hemolysis and dilution; the *Johansen et al.* patent (U.S. Patent No. 3,972,614, filed July 10, 1974), requires hemolysis by ultrasound; the *Loretz* patent (U.S. Patent No. 4,357,105, filed August 11, 1975), requires dilution. Each of these references are of record.

Each of these researchers (each of whom filed patent applications long after publication of the *Anderson et al.* article), avoided the known nonlinear functional relationship between optical density and hemoglobin concentration, by hemolyzing the blood, diluting the blood, or both. The only method that has been successful in spectrometering whole, undiluted blood to measure three or more constituent components, is Appellants' own. The failure of these researchers, as well as *Brown*, to analyze a whole blood sample to obtain three or more

components is illustrative of the non-obviousness of the subject invention.

The dependent method claims further define various optical arrangements (claims 2-10) and the interrelationship between each radiation frequency and the corresponding concentration of constituent components. Furthermore, not only is independent method claim 1 not obvious in view of *Anderson* and *Brown*, but dependent claims 2 and 6-12, which further limit claim 1, are non-obvious.

Claims 1 and 8-12 are separately patentable in view of *Anderson* and *Brown*. Neither *Anderson* or *Brown* make mention of light-emitting diodes (claim 8), controlled monochromators (claim 9), or controllable diffraction gratings (claim 10) as potential frequency sources. *Anderson* merely mentions that a Beckman DU spectrophotometer may be used as a light source (*Anderson* - page 176). Although *Brown* discloses interference filters (col. 2, lines 39-41) and laser sources (col. 2, lines 30-36), *Brown* does not suggest light-emitting diode sources, monochromator sources, or a controllable diffraction grating of separate and distinct claims 8-10 of the subject application. In fact, *Brown* teaches the advantages of hollow cathode lamps or lasers as the preferred choice.

In addition, neither *Anderson* nor *Brown* teach the relationship between radiation frequency and constituent components (claim 11), or that concentrations of at least three components using Beer-Lambert Law can be used (claim 12).

Accordingly, Appellants assert that claims 1 and 8-12 are separately patentable and non-obvious under *Anderson* and *Brown*, and that claims 1 and 8-12 do not stand or fall together.

### 3) Level of Ordinary Skill in the Art

The Graham inquiries point to the conclusion of non-obviousness of the present claims regardless of the presumed level of ordinary skill in the art. However, absent evidence to the contrary, a person of ordinary skill in the art is presumed to be one who essentially follows conventional wisdom and does not undertake to innovate. Standard Oil Co. v. American Cyanamid Co., 227 U.S.P.Q. 239 (Fed. Cir. 1985).

On the record of this case, one of ordinary skill in the art is one who must dilute and hemolyze the blood sample before he can obtain readings for three or more constituent components of blood. Otherwise, these skilled artisans can only obtain total hemoglobin concentration and oxygenated hemoglobin concentration when whole undiluted blood is used. The Final Rejection proposes that this routineer would take the whole blood measuring apparatus of *Anderson* and add three or more selected frequencies to obtain three or more constituent components of blood as in the present invention. This modified *Anderson* device -- which does not suggest a method of distinguishing each constituent component and minimizing scattering -- certainly cannot suggest the claimed method to an uninnovative person.

## II. Appellants' Claims 3-5 Are Not Rendered "Obvious" Under 35 U.S.C. § 103 Over the Examiner's Cited References

### a. The Examiner's Rejection Under 35 U.S.C. § 103

In rejecting claims 3-5 in the Final Office Action, the Examiner specifically stated:

> The use of such a large close detector [Shibata et al.] would have been obvious [in Anderson and Brown] because it is a known alternative method for obtaining the same desired result and does not require the additional presence of a integrating sphere.

### b. Appellants' Arguments/Response to Second Issue

*Anderson* and *Brown* references (which teach the problems of light scatter) in combination with *Shibata et al.* reference (which teaches an optic arrangement having a large area detector placed near the sample) does not render claims 3-5 "obvious" under 35 U.S.C. § 103.

In response to the Examiner's assertions, Appellants reassert the above arguments that *Anderson* and *Brown*, as proposed by the Examiner, do not meet the limitations of claim 1 combined with claims 3-5. Furthermore, *Shibata* deals with non-analogous art, separate and distinct from blood analyzers of *Brown* and *Anderson*. Consequently, *Shibata* does not cure the incompatibility of the *Anderson* and *Brown* teachings.

The purpose of the *Shibata* reference is to overcome certain undesirable properties of photomultiplier tubes by more evenly

distributing light over the face of the detector surface. This is achieved by using a light diffusing plate, which in turn necessitates placing the detector close to the sample. *Shibata* has nothing to do with whole-blood spectrometric methods of the present art. *Shibata* reference is not within the field of the present claimed art, nor is it reasonably pertinent to the unique problems with which the claimed invention is involved. See In re Wood, 599 F.2d 1032, 1036, 202 U.S.P.Q. 171, 174 (C.C.P.A. 1979).

In addition, absent Appellants' disclosure, there is absolutely no basis or motivation in the teachings of the prior art to apply the *Shibata* structure to the combination of *Anderson* and *Brown* absent some teaching, suggestion of incentive supporting the combination. ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984). Absent such a showing in the prior art, the Examiner cannot impermissibly use the Appellants' teaching to hunt through the prior art for the claimed elements and combine them as claimed. In re Laskowski, 871 F.2d 115, 117 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989).

In light of the foregoing remarks, Appellants assert that improper combination of nonanalogous art cannot render dependent claims 3-5 obvious. Furthermore, the base claim (claim 1) from which claims 3-5 are dependent therefrom is certainly not shown in the hypothetical combination of *Anderson*, *Brown* and *Shibata*. In particular, since neither *Anderson*, *Brown* nor *Shibata* disclose or suggest optical detectors which minimize scattering and

distinguish blood components of claims 3-5 in combination with claim 1, Appellants assert that claims 3-5 are non-obviousness in view of the hypothetical combination.

## D. CONCLUSION

It is contended that the Examiner erroneously rejected Appellants' claims as obvious under 35 U.S.C. § 103. A proper Graham analysis reveals that a significant difference exists between the scope and content of the prior art and the present claims at issue.

Accordingly, in light of the foregoing comments, Appellants respectfully request the Board of Patent Appeals to reverse the Examiner's rejection of claims 1-12.

Respectfully submitted,

Kevin L. Daffer
Reg. No. 34,146

ARNOLD, WHITE & DURKEE
P.O. Box 4433
Houston, Texas 77210
(512) 320-7200

Dated: 7/26/91

## 7. APPENDIX

A copy of the claims involved in the present appeal include the following:

1. A method of determining concentrations of constituent components of whole undiluted blood, including:

generating a plurality of radiation frequencies each determined to distinguish one said constituent component from another said constituent component, and to minimize the effect of radiation scattering and to maximize radiation absorbance by whole, undiluted blood;

irradiating a sample of whole, undiluted blood with at least three of said radiation frequencies, through a depth of said sample chosen to minimize radiation scattering by whole, undiluted blood;

detecting intensities of said radiation frequencies, after passing through said depth of said sample, at a distance from said sample, and over a detecting area, both chosen to minimize the effect of radiation scattering by whole, undiluted blood; and

calculating concentrations of each of at least three said constituent components of said sample of whole, undiluted blood, based upon detected intensities of said radiation frequencies, and upon predetermined molar extinction coefficients for each of said

constituent components at each of said radiation frequencies.

2. A method as recited in claim 1, wherein said depth of said sample is in the range of 80 to 150 micrometers.

3. A method as recited in claim 1, wherein said detecting area is at least approximately 600 square millimeters.

4. A method as recited in claim 3, wherein said distance from said sample is within the range of 2 to 10 millimeters.

5. A method as recited in claim 1, wherein said step of detecting is performed over a half-aperture angle of radiation emanating from said sample of at least approximately 70°.

6. A method as recited in claim 1, wherein said step of generating further comprises the steps of:

generating white light; and

passing generated white light through a plurality of interference filters, corresponding to said plurality of radiation frequencies.

7. A method as recited in claim 1, wherein said step of generating further comprises the steps of:

providing a tunable source of laser radiation; and

selectively tuning said tunable source of laser radiation to each of said plurality of radiation frequencies.

8. A method as recited in claim 1, wherein said step of generating further comprises the steps of:

generating light using light-emitting diodes; and

passing light generated by said light-emitting diodes through a plurality of interference filters corresponding to said plurality of radiation frequencies.

9. A method as recited in claim 1, wherein said step of generating further comprises the steps of:

generating white light; and

passing generated white light through a controllable monochromator to selectively produce each of said plurality of radiation frequencies.

10. A method as recited in claim 1, wherein said step of generating further comprises the steps of:

generating white light; and

passing generated white light through a controllable diffraction grating to produce said plurality of radiation frequencies.

11. A method as recited in claim 1, wherein said radiation frequencies are equal in number to said constituent components.

12. A method as recited in claim 11, wherein said step of calculating comprises calculating concentrations of each of at least three said constituent components using the Beer-Lambert Law of absorption spectroscopy.

*g:\utsk\097\app\01.daf*